

REMARKS:

In the foregoing amendments, Applicant amends claim 1 by changing the temperature range from “less than 75°C” to “10°C to 60°C,” which temperature range is discussed in the Specification at page 6, lines 1-6. Claims 1 and 3 remain in the application for consideration by the Examiner. Applicant respectfully requests and allowance of these claims for the following reasons.

The outstanding Final Office Action withdrew the two prior art rejections in the previous Office Action. These included the rejection under 35 U.S.C. §102(b) over Choudary (US 6,274,741) and the rejection under 35 U.S.C. §103(a) over Davis (PCT/US00/30205, published as WO 01/32593) and Hartough (US 2,458,519). Unfortunately, the outstanding Final Office Action included a new rejection of claims 1 and 3 under 35 U.S.C. §103(a) as being unpatentable over Norton (US 2,711,414) in view of Chakrabarti (*Reactive Polymers*, 20, pp. 1-45, 1993). Since Applicant has not yet had an opportunity to respond to the new ground of rejection, Applicant respectfully requests that the foregoing amendment be entered and the attached Rule 132 Declaration be considered by the Examiner under the provisions of 37 C.F.R. §1.116(b) for the purposes of placing the application in condition for allowance or for the purposes of appeal.

Present claims 1 and 3 define, *inter alia*, a process for the preparation of a 2-acylthiophene compound which comprises reacting a thiophene of formula (1) with acid anhydrides represented by formula (2) or acid halides represented by formula (3) in the presence of a cation exchange resin at a temperature of 10°C to 60°C in the absence of solvent, thus producing a 2-acylthiophene compound represented by formula (4). The teachings of Norton and Chakrabarti, either alone or in combination, do not contemplate or suggest the process defined in claims 1 and 3 within the meaning of 35 U.S.C. §103(a).

Applicant discovered that a specific reaction temperature in the range of 10°C to 60°C can reduce the 3-isomer content as a byproduct, which had been a problem in the conventional process of producing 2-acetylthiophene, while also improving the yield of 2-acetylthiophene. The attached declaration under 37 C.F.R. §1.132 of Seiji Bando (“Bando declaration”) demonstrates that, when the presently claimed reaction was carried out at temperatures of 30°C, 40°C, and 60°C; the 3-acetylthiophene content in the 2-acetylthiophene was 0.3 wt%, 0.4 wt%, and 0.5 wt%, respectively (i.e., the 3-thiophene isomer content was very low). However, when the reaction temperature was as high as 100°C, which is outside the presently claimed range, the 3-acetyl thiophene content of the resulting

the 2-acetylthiophene was 0.9 wt% (i.e., the 3-isomer content as a byproduct was very high).

The Office Action stated that Norton teaches that thiophene can be effectively acylated without solvent in a temperature range of 75-125°C with cationic exchange resins. The Office Action stated that Chakrabarti teaches that cationic exchange resins often improve product yield and purity when used in organic reactions over other catalyst. Applicants respectfully submit that the Office Action statement that Chakrabarti teaches that cationic exchange resins are effectively used to improve product purity and yield with reduced cost over other catalyst is overly broad and cannot provide reasons to one of ordinary skill in the art to understand that the presently claimed invention would necessarily have improved or unexpected results. By their very nature, catalysts have no predictability. Chakrabarti does not teach that cationic exchange resins provide superior results for all types of organic reactions and, in fact, discusses many limitations of ion exchange resins as catalyst (Chakrabarti pp. 7-8). Furthermore, Applicant cannot find a specific discussion in Chakrabarti concerning the acylation of thiophene. Therefore, Applicant can find no reason in Chakrabarti for one of ordinary skill in the art to expect an improved or superior reaction product by the

use of cationic exchange resins, especially at a temperature of 10°C-60°C, in the process defined by the present claims.

The Office Action included the following comments in support of its position of obviousness:

- (1) Chakrabarti et al. teach that cationic exchange resins are effective at replacing traditional mineral acids and bases in organic reactions, as reaction rates are often higher and lower reaction temperatures are necessary (p. 6, ll. 18-21).
- (2) Chakrabarti et al. teach that product purity and yield are often improved when the catalysts employed are cationic exchange resins (p. 7, ll. 3-5).
- (3) Thiophene has a boiling point of 84°C, and therefore the acylation reaction could reasonably be conducted at this temperature (the boiling point of thiophene). Additionally, it would be obvious for one of ordinary skill in the art to optimize the reaction conditions, such as determining specific cationic resins and reaction pressure ranges... (p. 7, ll. 7-10).
- (4) [I]t is known in the art that a lower reaction temperature results in less decomposition of products, thereby increasing purity (p. 7, ll. 12-13).

Concerning comments (1) and (2) of the Office Action, while Chakrabarti discusses or proposes organic reactions of ketones with alcohols to produce ketals, Chakrabarti does not teach any specific reaction system related to the presently claimed method, i.e., reaction of a thiophene compound with acid anhydrides or acid halides (Chakrabarti p. 2, left column, l. 25, to right column, l. 3).

Furthermore, Chakrabarti nowhere teaches specifically what reaction system and what reaction conditions are required to improve purity and reaction yields. In fact, as can be clearly seen from the attached Bando declaration, the 3-acetylthiophene content as a byproduct varies depending on the reaction temperature, even when the same cationic exchange resin is used. At least for these reasons, Applicant respectfully submits that the teachings of Chakrabarti provide no reason for one of ordinary skill in the art to modify the acylation reaction temperatures of 75°C to 125°C as required in Norton to the presently claimed temperature range of 10°C to 60°C.

In addition, while Table 3 of Chakrabarti (pp. 13-23) lists various types of cationic exchange resins and organic reactions using cationic exchange resins as catalysts, this table fails to specifically describe or suggest a reaction for the acylation of a thiophene compound. Nowhere does Chakrabarti address how to solve the problem of forming a structural isomer, which occurs after a reaction as in the substitution reaction of a thiophene compound as a starting material of the presently claimed invention. At least for these reasons, Applicant respectfully submits that the teachings of Chakrabarti provide no reason for one of ordinary skill in the art to modify the acylation reaction temperatures of 75°C to 125°C as required in Norton to the present claim temperature range of 10°C to 60°C.

The Office Action acknowledged that Norton proposes that the acylation occurs at reaction temperatures of 75°C to 125°C. On the other hand, the presently claimed invention requires a reaction temperature range of 10°C to 60°C, which is completely outside the range proposed by Norton. It cannot be obvious to one of ordinary skill in the art to completely disregard the reaction temperature range proposed by Norton and substitute a completely different range therefor. Norton itself teaches away from such a substitution. Along these lines, it is respectfully noted that the boiling point of 84°C for thiophene, as alleged in the above comment (3) of the Office Action, is also completely outside the presently claim range of 10°C to 60°C. At least for these reasons, Applicant respectfully submits that the Office Action provides no reason in the rejection that explains why one of ordinary skill in the art would utilize the presently claimed range of 10°C to 60°C in the manner required in Applicant's claims.

Concerning comments (4) of the Office Action concerning "decomposition of products," Applicant respectfully submits that those skilled in the art understand that the isomer substituted at position 3 of thiophene is not produced as a result of the decomposition of products, but as a result of a reaction at position 3 of thiophene with acid anhydrides or acid halides. Accordingly, any knowledge of a person of ordinary skill in the art concerning the "decomposition of products"

provides no reason for one of ordinary skill in the art to utilize the lower reaction temperatures of 10°C to 60°C, as required in the present claims, within the teachings of Norton.

In addition, Norton completely fails to recognize any problem associated with the 3-isomer content of a thiophene compound, which increases when the reaction temperature is high. Consequently, Norton, which proposes a reaction temperature of 75°C to 125°C, nowhere contemplates or suggests that the 3-isomer content of a thiophene compound can be reduced by using a low reaction temperature range from 10°C to 60°C, as presently claimed.

The attached Bando declaration establishes the unexpected advantages of the presently claimed invention, and thereby rebuts any alleged prima facie case of obviousness over Norton and Chakrabarti. As shown in the declaration, when the reaction was carried out at temperatures of 30°C, 40°C, and 60°C as presently claimed, the 3-acetylthiophene content in the 2-acetylthiophene was 0.3 wt%, 0.4 wt%, and 0.5 wt%, respectively (namely, the 3-thiophene isomer content was very low). On the other hand, when the reaction temperature was as high as 100°C, such as proposed by Norton, the 3-acetyl thiophene content of the resulting 2-acetylthiophene was 0.9 wt% (namely, the 3-isomer content as a byproduct was very high). The presently claimed method by the use of a cation exchange resin at

a temperature range of 10°C to 60°C can unexpectedly reduce the 3-isomer content as a byproduct, which had been a problem in the conventional process of producing 2-acetylthiophene. In addition, the presently claimed invention also improves the 2-acetylthiophene yield.

For at least the foregoing reasons, Applicant respectfully submits that the inventions defined in claims 1 and 3 are not contemplated or suggested by, and thus are patently distinguishable from, the teachings of Norton and/or Chakrabarti. Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection under U.S.C. §103(a) that was set forth in the outstanding Office Action.

Applicant believes that the foregoing is a complete and proper response to the Office Action mailed May 11, 2009. While it is believed that all pending claims in this application are in condition for allowance, if the Examiner has any comments or questions, Applicants invite the Examiner to telephone the undersigned to resolve any outstanding issues at the below listed number.

In the event that this paper is not timely filed, Applicant hereby petitions for an appropriate extension of time. The Commissioner is hereby authorized to charge the fee therefor, as well as any deficiency in the payment of the required fee(s) or credit any overpayment, to our deposit account No. 50-1147.

Respectfully submitted,
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